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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,384	01/11/2001	Hau H. Duong	A-68718-2/RFT/RMS/RMK	2482

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EXAMINER	
SINES, BRIAN J	
ART UNIT	**PAPER NUMBER**
1743	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,384	DUONG ET AL.	
	Examiner	Art Unit	
	Brian J. Sines	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-27,29-36 and 38-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-27,29-36 and 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 24 – 27, 29 – 31, 33, 34, 41 & 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holen et al. (U.S. Pat. No. 5,320,808 A) (hereinafter "Holen") in view of Eggers et al. (U.S. Pat. No. 5,532,128 A) (hereinafter "Eggers").

Holen teaches a semi-automated sample analyzer and subsystems for simultaneously performing a plurality of immunoassays utilizing reaction cartridges. A carousel is provided to position and hold a plurality of reaction cartridges. Each cartridge includes a plurality of isolated test sites formed in a two-dimensional array in a solid-phase binding layer contained within a reaction well, which is adapted to contain a biological sample to be assayed (see Abstract).

Regarding claims 24, 41 and 42, Holen teaches the recited methodology of analyzing a plurality of biochips, wherein the method is comprising the steps of:

(a) inserting a first biochip (reaction cartridge 80) into a first station (opening 98 on carousel 18) of an analysis device (10);

(b) inserting a second biochip into a second station of the analysis device, wherein each of the first and second biochips comprise a substrate (test card 82) comprising an array comprising a plurality of test sites (84), wherein each test site (84) is comprising:

i) a different capture binding ligand (e.g., a capture reagent, such as antibodies, antigens, anti-biotin, avidin, lectins, peptide sequence probes or specific allergen which binds human IgE class antibodies from a patient serum sample);

ii) a different target analyte (e.g., a specific binding component, such as antigens from a patients sample, such as from serum, blood, urine, cerebrospinal fluid (CSF) or saliva); and

iii) a label (e.g., a human IgE class antibody conjugated to an enzyme, such as alkaline phosphatase or horse radish peroxide (HRPO) conjugate, or any other detectable enzymatic or fluorogenic conjugate);

(c) detecting the presence of the label on the first biochip utilizing optical reader (32) from the test sites (84) from the reaction cartridge (80); and

(d) detecting the presence of the label on the second biochip (see col. 6, line 10 – col. col. 20, line 38; figures 2, 3 & 5).

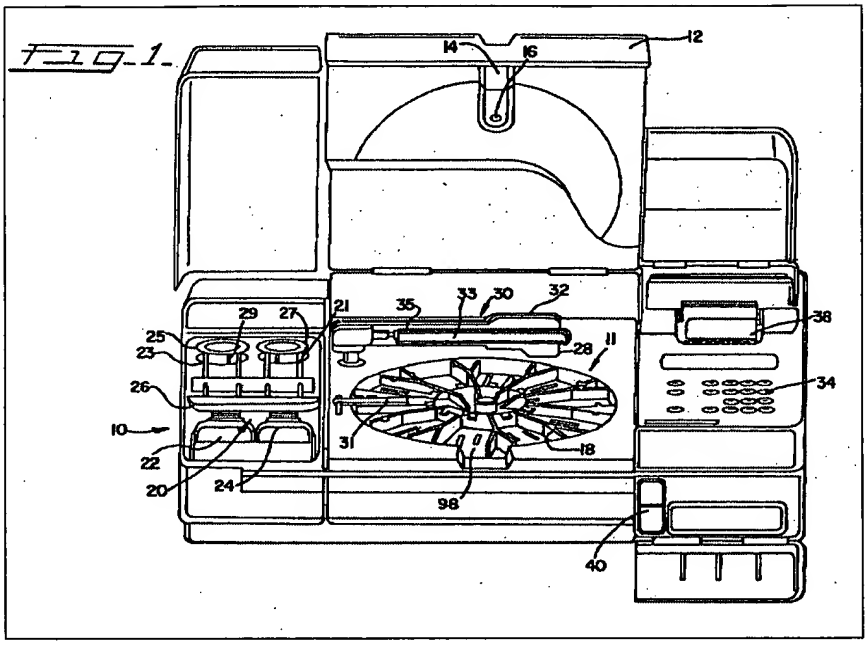
Fig. 1.
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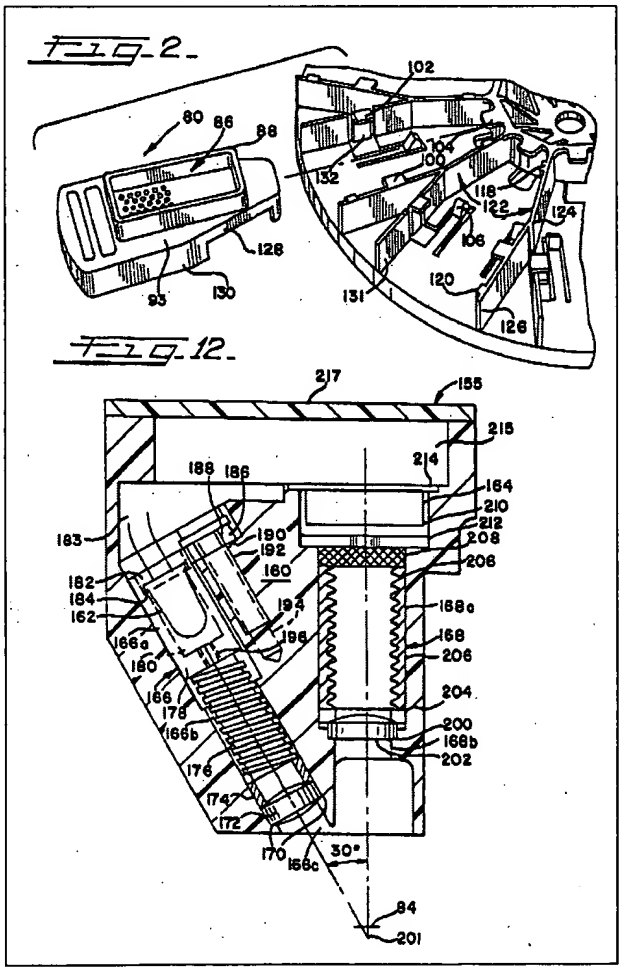
Fig. 2.
102
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Fig. 12.
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162
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188a
196
168
206
166a
180
204
166
178
200
166b
168b
202
176
174
172
170
156c
30°
84
201

Fig. 3.

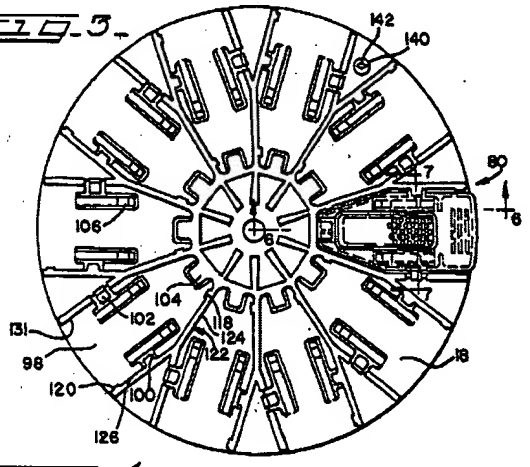


Fig. 4.

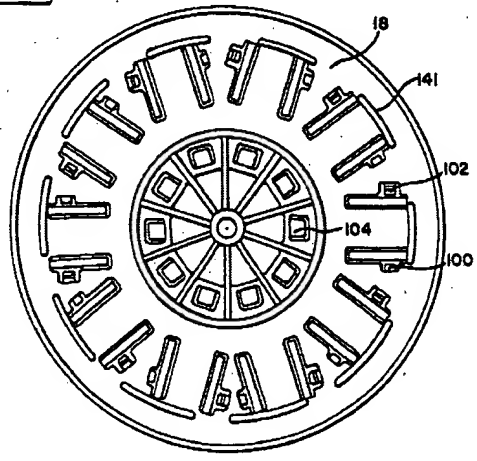
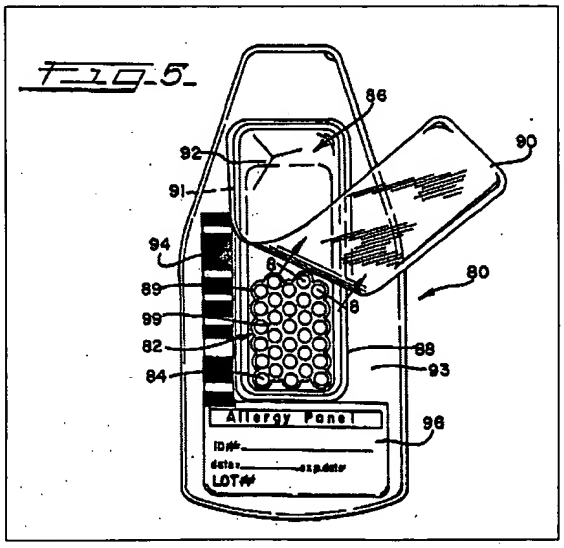


Fig. 5.



Although Holen does not specifically teach the further incorporation of an array of detection electrodes further comprising a plurality of electrical contacts. Eggers teaches a multi-site electronic detection apparatus comprising a plurality of test sites (14) comprising a well (20), which comprises a plurality of electrode pairs (24a & 24b) for the analysis of biological samples (see col. 3, line 54 – col. 4, line 60; figures 1 – 3). Eggers teaches that the detection apparatus further comprises detection circuitry (16) and recognition circuitry (18), which monitors and controls the apparatus (see col. 3, lines 51 – 67).

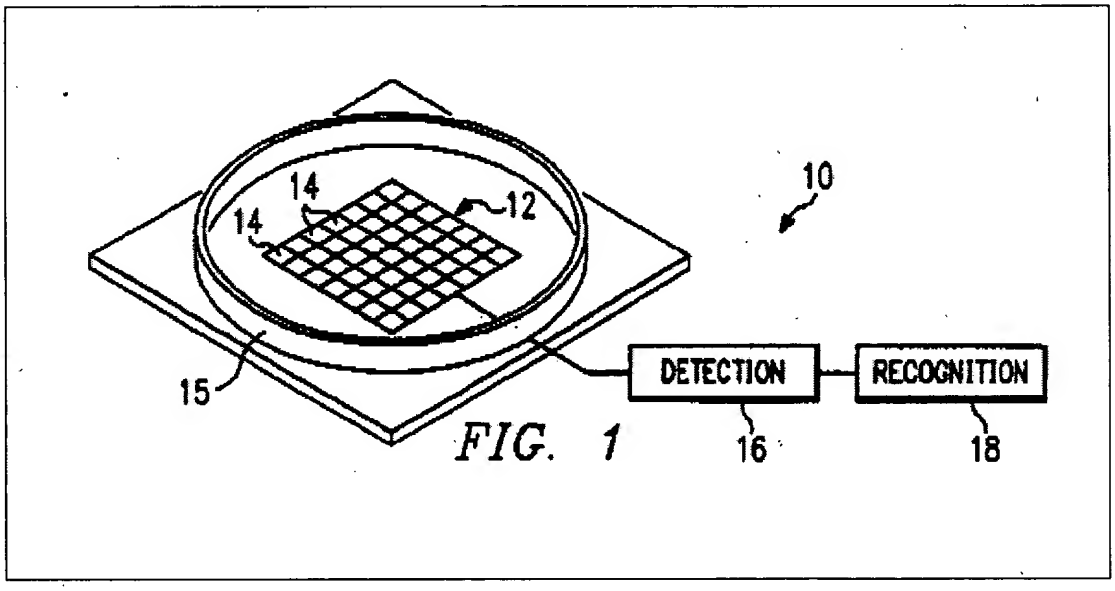


FIG. 1

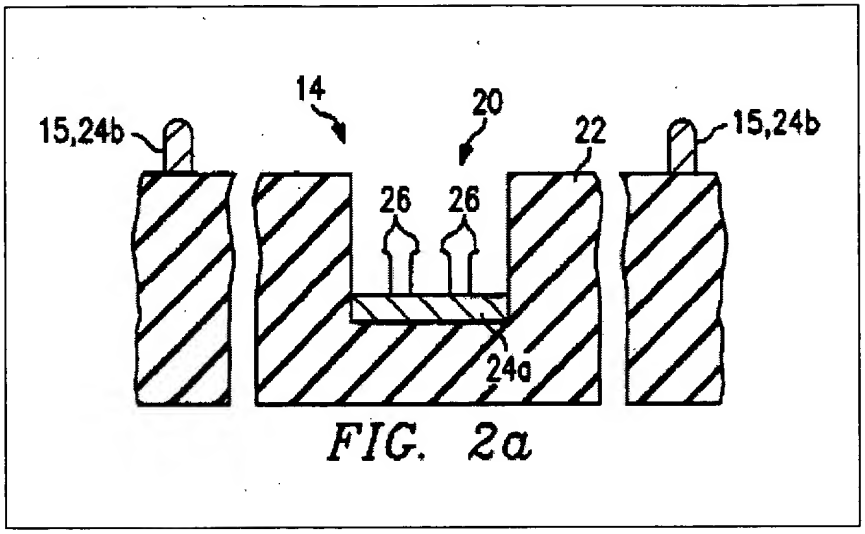


FIG. 2a

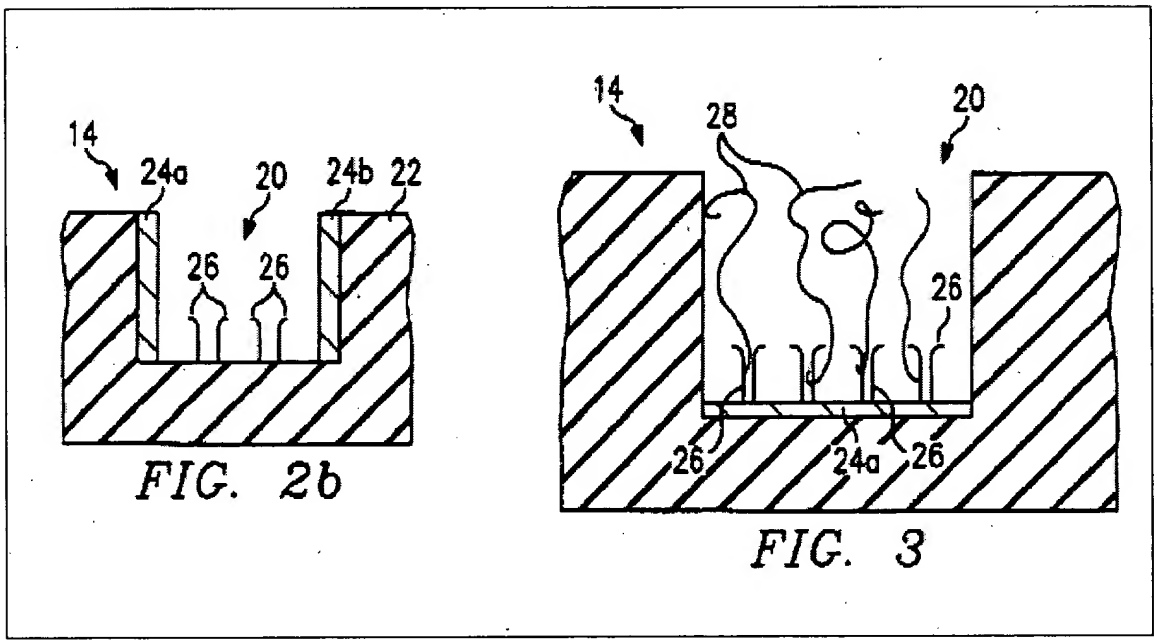


FIG. 2b

FIG. 3

Eggers teaches the advantages of the disclosed electronic detection apparatus and methodology in relation to optical detection methods utilizing fluorescent labels and including intercalating dyes for DNA analysis (see col. 2, lines 1 – col. 3, lines 26). Eggers further teaches the increased sensitivity afforded by the disclosed electronic detection apparatus and methodology (see col. 3, lines 11 – 25). The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning

based on established scientific principles or legal precedent, that some advantage, or expected beneficial result would have been produced by their combination. See *In re Sernaker*, 702 F.2d 989, 994 – 995, 217 USPQ 1, 5, 6 (Fed. Cir. 1983) (see MPEP § 2144). In addition, as evidenced by Eggers, a person of ordinary skill in the art would accordingly have had a reasonable expectation for success of utilizing such an electronic detection system and methology for the analysis of biological samples. The Courts have held that the prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. See *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (see MPEP § 2143.02). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate an electronic detection system, as taught by Eggers, within a biological sample analyzer and sample analysis methodology as recited in claim 24, in order to facilitate efficient and effective biological sample analysis, and which could also utilize either electronic or optical detection, or both detection methods.

Regarding claims 25 and 26, Holen teaches that the rotatably-mounted optical reader arm (35) is moved over each reaction cartridge (80). Holen teaches that under microprocessor control, the carousel (18) and optical reader arm (35) move in cooperation to sequentially position the optical reader (32) over each selected test site (84) until all selected test sites have been read (see col. 8, lines 4 – 35; col. 17, line 26 – col. 18, line 66).

Regarding claim 27, neither Holen nor Eggers specifically teach the incorporation of a plurality of detectors within the system. Although Holen does teach the incorporation of a single optical reader or detector in determining assay results (see e.g., col. 8, lines 4 – 35). The Courts have held that the mere duplication of parts, without any new or unexpected results, is

within the ambit of one of ordinary skill in the art. See *In re Harza*, 124 USPQ 378 (CCPA 1960) (see MPEP § 2144.04). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate a plurality of detectors within the analyzer system, as taught by Holen, to facilitate the detection and analysis of the plurality of reaction cartridges used within the system.

Regarding claim 29, Holen teaches the use of an electronic detector, e.g., a solid-state device, i.e., light-emitting diode (LED) (see col. 20, lines 25 – 38). In addition, Eggers teaches electronic detection (see col. 3, line 51 – col. 4, line 66; col. 5, lines 44 – 67).

Regarding claims 30, 31 & 33, Holen does not specifically teach that the capture binding ligands are nucleic acid probes, the target analytes are target nucleic acid sequences and the assay complexes are hybridization complexes. Holen does indicate that the disclosed system can be utilized for DNA hybridization capacity studies (see col. 13, lines 34 – 57). As evidenced by Eggers, the electronic detection of nucleic acids using electrodes is well known in the art. Eggers teaches that the disclosed electronic detection technique can be utilized to detect target DNA using DNA probes (see col. 5, lines 44 – 66). Eggers teaches that the disclosed apparatus and electronic detection technique enables fast detection for large DNA probe arrays (see col. 7, lines 31 – 44). Consequently, a person of ordinary skill in the art would accordingly have had a reasonable expectation of success of incorporating the use of nucleic acid hybridization assays with the system and methodology taught by Holen and Eggers. Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the use of DNA hybridization assays with the system and methodology taught by Holen and Eggers.

Regarding claim 34, Eggers teaches that the use of intercalating dyes are known in the art of optical detection (see col. 3, lines 11 – 26). The Courts have held that the selection of a known material, which is based upon its suitability for the intended use, is within the ambit of one of ordinary skill in the art. See *In re Leshin*, 125 USPQ 416 (CCPA 1960) (see MPEP § 2144.07).

2. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Holen in view of Eggers, as applied to claims 24 – 27, 29 – 31, 33, 34, 41 & 42 above, and further in view of Yabusaki et al. (U.S. Pat. No. 4,599,303) (hereinafter "Yabusaki").

Holen and Eggers do not specifically teach the use of labels covalently attached to the target sequences. Yabusaki does teach a method wherein probes or labels are covalently attached to the target nucleic acid sequence. Yabusaki teaches a method of identifying specific nucleic acid sequences in which the target nucleic acid sequence is reacted with a probe or label under conditions where hybridization of the probe with the target sequence will occur. Following hybridization, the sample is subjected to a photochemical or chemical procedure, which causes covalent crosslinking of the probe to the target complementary sequence. Following cross-linking, the uncrosslinked probe is separated from the covalently crosslinked probe-target complex (see col. 2, lines 24 – 68; col. 3, lines 1 – 23). As evidenced by Yabusaki, a person of ordinary skill in the art would accordingly have recognized the suitability of incorporating this disclosed methodology of detecting target nucleic acid sequences with the methodology of Holen and Eggers for the intended purpose of providing for an effective means for facilitating the sensitive detection of extremely low concentrations of specific nucleic acid base sequences (see MPEP § 2144.07). Furthermore, as disclosed by Yabusaki et al., a person of ordinary skill in the art would accordingly have had a reasonable expectation of success of incorporating such a

methodology for facilitating the effective detection of target nucleic acid sequences. Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the method disclosed by Yabusaki et al., with the method of Holen et al. and Eggers in order to provide an effective means for detecting target nucleic acid sequences.

3. Claims 35, 36, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holen and Eggers, as applied to claims 24 – 27, 29 – 31, 33, 34, 41 & 42 above, and further in view of Meade et al. (U.S. Pat. No. 5,780,234 A) (hereinafter "Meade").

Regarding claims 35, 36 and 38, Meade teaches hybridization complexes essentially comprising: capture probes hybridized to a first domain of a target sequence; and label probes, e.g., covalently attached electron transfer moieties, hybridized to a second domain of the target sequence (see col. 5, line 29 – col. 6, line 62). Regarding claims 38 and 39, neither Holen nor Eggers specifically teach the use of electron transfer moieties, such as transition metal complexes, as labels. Meade does teach the use of electron transfer moieties (ETM's), such as transtion metal complexes as labels or probes for assays (see col. 7, lines 14 – 67; col. 8, lines 1 – 67; col. 10, lines 44 – 59). Hence, as evidenced by Meade, a person of ordinary skill in the art would have recognized the suitability of using the teachings of Meade regarding the use of electron transfer moieties and transition metal complexes as labels or probes for the intention of performing hybridization assays (see MPEP § 2144.07). In addition, the Courts have held that the selection of a known material, based upon its suitability for the intended use, is within the ambit of one of ordinary skill in the art. See *In re Leshin*, 125 USPQ 416 (CCPA 1960) (see MPEP § 2144.07). Furthermore, Meade does teach that their disclosed technique is suitable for automated probe assays (see col. 8, lines 62 – 67). It is well known in the art to detect samples

containing ETM's using both electronic and optical detection methods. Consequently, a person of ordinary skill in the art would accordingly have had a reasonable expectation of success of incorporating the teachings of Meade with the system and methodology of Holen and Eggers. Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the teachings of Meade with Holen and Eggers in order to provide for an effective detection method.

4. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Holen, Eggers & Meade, as applied to claims 35, 36, 38 & 39 above, and further in view of Grinstaff et al. (U.S. Pat. No. 6,288,221 B1) (hereinafter "Grinstaff").

Holen, Eggers and Meade do not specifically teach the use of metallocenes. Grinstaff et al. do teach the use of a metallocene in methods for detecting nucleic acid sequences (see col. 9, lines 27 – 46; col. 42, lines 27 – 37). Hence, as evidenced by Grinstaff, a person of ordinary skill in the art would have recognized the use of metallocenes as a component of a detectable marker in a methodology for detecting target nucleic acid sequences. The Courts have held that the selection of a known material, based upon its suitability for the intended use, is within the ambit of one of ordinary skill in the art. See *In re Leshin*, 125 USPQ 416 (CCPA 1960) (see MPEP § 2144.07). Furthermore, since both Holen and Grinstaff rely on optical methods for detection, a person of ordinary skill in the art would accordingly have had a reasonable expectation of success of incorporating the use of a metallocene transition metal complex with the methods disclosed by Holen (see Holen: col. 19, line 65 – col. 20, line 38; Grinstaff: col. 11, lines 26 – 65). Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the use of a metallocene transition metal complex, as taught by Grinstaff et al., with the

methodology of Holen, Eggers and Meade in order to facilitate the effective detection of target nucleic acid sequences.

Response to Arguments

Applicant's arguments with respect to the pending claims have been considered, but are moot in view of the new ground(s) of rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Sines, Ph.D. whose telephone number is (571) 272-1263. The examiner can normally be reached on Monday - Friday (11 AM - 8 PM EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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